

ORIGINAL ARTICLE

Accuracy of Power Mode Transcranial Doppler in the Diagnosis of Brain Death



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Background: The diagnosis of brain death (BD) is complex. For this reason, we aimed to evaluate the accuracy of power mode transcranial Doppler (PMD-TCD) in diagnosing BD.

Patients and methods: Patients admitted to an intensive care unit between December 2003 and January 2012 were included in this study if they were in a structural coma, had no craniectomy, and were evaluated blind by a neurologist using PMD-TCD. The diagnosis of BD was based on an evaluation that took into consideration the absence of sedative drugs, a median blood pressure >60 mmHg, a body temperature >35°C, and the absence of brainstem reflexes. A neurosonologist followed a protocol using PMD-TCD that considered the examination as positive for brain circulatory arrest given the presence of reverberating, small systolic peaks or the disappearance of a previous signal present in both middle cerebral arteries and intracranial vertebral arteries.

Results: A total of 74 patients were evaluated. In 61 (82.4%) patients the interval between both evaluations was less than 1 hour. The sensitivity and specificity for the diagnosis of BD

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with PMD-TCD were 100% and 98%, respectively. The positive and negative likelihood ratios for BD were 45 and 0, respectively.

Conclusion: PMD-TCD is accurate for the diagnosis of BD.

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Introduction

In many countries, clinical examination is the gold standard for the confirmation of brain death (BD) [1,2]. However, in some patients, face or chest injuries do not allow the evaluation of brainstem reflexes or the performance of an apnea test [3]. In these patients, additional tests are required to confirm brain circulatory arrest. Some of these tests, such as angiographic or radionuclear cerebral flow studies, are expensive and cannot be performed in some hospitals [4]; other studies, such as computed tomography angiography, may produce false positive results [5].

Transcranial Doppler (TCD) is a noninvasive, safe, and bedside technique used to evaluate blood flow velocity in the basal arteries of the brain. A published meta-analysis has reliably confirmed its accuracy in cerebral circulatory arrest, with a sensitivity of 89% and a specificity of 99%. The studies included in this meta-analysis used single-gate TCD for the diagnosis of BD [6].

A new ultrasound technology, power mode transcranial Doppler (PMD-TCD), uses 33 overlapping Doppler samples to simultaneously display flow signal intensities and direction over 6 cm of intracranial space to assist in the search for intracranial arteries [7]. The advantages of PMD-TCD over single-gate TCD in detecting acoustic windows have been described previously [8]. A single small study has suggested a high accuracy for PMD-TCD in the diagnosis of BD [9].

In this study, we evaluated the diagnostic accuracy of PMD-TCD compared with clinical neurological examination as a standard for diagnosing BD in patients with structural coma (SC) in an intensive care unit (ICU).

Patients and methods

This prospective study was performed in the ICU of the Clínica Alemana of Santiago, Chile from December 2003 to January of 2012. Consecutive patients were included if they met the following criteria: the patient was in an SC and was suspected to be BD according to the intensive care doctor on call; the patient had not undergone a craniectomy or ventricular drain; and a neurological evaluation as well as a PMD-TCD ultrasound examination was performed with an interval of less than 3 hours between them and with blind results for each evaluator. Patients were excluded if they did not meet these criteria.

The diagnosis of BD was made by the neurologist on call using the criteria according to Chilean law, which is based on a clinical evaluation that considers the absence of sedative drugs, a median blood pressure >60 mmHg, a body temperature >35°C, and the complete absence of brainstem reflexes [10].

PMD-TCD was performed by an experienced sonographer (A.B.) who is certified by the American Society of Neuroimaging Ultrasound. A Power Motion PMD-100 Spencer Technologies device with a 2 MHz probe and a 6–9-mm sample volume at a power setting of 100 and a filter of 200 was used. The institutional protocol declares brain circulatory arrest in the presence of reverberating, small systolic peaks or the disappearance of a previous flow signal in both middle cerebral arteries (MCA) through the transtemporal window at a depth of 55 mm and through both vertebral arteries identified via insonating through the transforaminal window at a depth of 60 mm [11].

In the patients for whom there was an acute increase in intracranial pressure, PMD-TCD was extended for more than 30 minutes and all arteries were re-evaluated.

The study protocol was reviewed and approved by the Institutional Ethics and Scientific Committee.

Statistical analysis

We calculated the likelihood ratios, sensitivity, specificity [12], and diagnostic accuracy of PMD-TCD in detecting BD among the patients who were in an SC.

Results

During this prospective study, 111 consecutive patients in a SC were admitted to the ICU of the Clínica Alemana Santiago; 74 of these patients were included in the protocol and, of these, 30 patients were classified as brain dead. Fig. 1 shows the criteria for exclusion from the analysis and Table 1 lists the characteristics of this group of patients. The mean \pm SD (range) time interval between the clinical evaluation and PMD-TCD was 84.8 ± 51.8 (5–178) minutes. The interval between the evaluations was less than 1 hour in 61 (82.4%) patients. The PMD-TCD was performed before the clinical evaluation in 27 (36.4%) patients. The sensitivity and specificity of the diagnosis of BD using PMD-TCD were 100% and 98%, respectively, and the positive and negative likelihood ratios for BD were 49 and 0, respectively. Fig. 2 is an example of flow arrest detected using PMD-TCD.

The only false positive result obtained using PMD-TCD involved a 90-year-old man who arrived at the emergency room in a coma with a Glasgow coma score of 3. His brain computed tomography scan showed a massive cerebellar hemorrhage. He was mechanically ventilated with no sedation. PMD-TCD was performed at 85 minutes of evolution and showed reverberating flow signals in both MCA at 55 mm depth, and in the vertebral arteries. A clinical evaluation performed 15 minutes later showed fixed pupils,

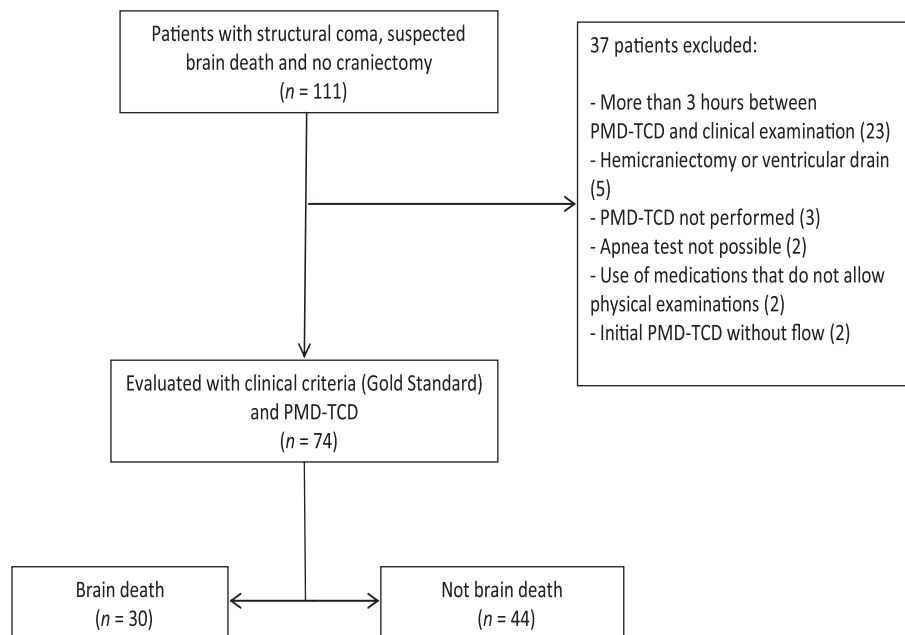


Fig. 1 Patients excluded from the analysis.

no response to pain, no oculomotor reflexes, and no corneal reflexes; however, he had weak breathing movements at 1 minute during the apnea test. The clinical evaluation was repeated after 6 hours. The patient was declared brain dead at this time.

Discussion

Our study shows that PMD-DTC is accurate in detecting BD patients in a SC with a sensitivity of 100% and a specificity of 98%. More importantly, PMD-TCD had a diagnostic accuracy of 98.6 and a positive likelihood ratio that was clearly >10 , which indicates a large and often conclusive increase in the likelihood of BD. The negative likelihood ratio of 0 indicates a negative probability of BD when circulation

was detected using PMD-TCD. PMD-TCD improves the pre-test probability (prevalence) of 0.40 by a posttest odds of 30.

As with the series of patients reported by Garamy et al [9], our results with PMD-TCD represent an improvement compared with those achieved with single-gate TCD. A meta-analysis reported by Monteiro et al [6] had a sensitivity of 89% and a specificity of 99%.

Compared with single-gate TCD, where flow must be identified at one depth level, which could be extremely difficult in patients in whom the brain blood flow is minimal and/or the brain vessels could have shifted (as a result of the mass effect of the lesions causing the SC), PMD-TCD integrates 33 overlapping Doppler samples and simultaneously displays flow signals and direction in a 6-cm segment of intracranial space, thus serving as a guide for the determination of minimal blood flow. Compared with single-gate TCD, PMD-TCD has been shown to improve the diagnostic accuracy of posterior circulation cerebral ischemia, as well as the detection of acoustic windows and microembolic signatures [8,13,14].

The search for cerebral flow in arteries of anterior and posterior circulation, could also explain the accuracy of our results. Some TCD studies, such as that by Feri et al [15], evaluated arteries of the anterior circulation only, with a sensitivity for detecting BD of 81.8%. Petty et al [16] and Zurynski et al [17], who analyzed the circulation of both arterial territories, achieved sensitivities that did not exceed 95% using single-gate TCD. Table 2 compares our study with those of other workers using single-gate devices.

Only one of our patients gave a false positive result and this was probably because the test was performed very early in his evolution. It has been suggested that very early ultrasound studies could be less accurate in the diagnosis of BD [21]. Posterior cranial fossa lesions that compress the brainstem do not follow the classic sequence of rostrocaudal deterioration of supratentorial lesions with

Table 1 Characteristics of patients classified as brain dead and not brain dead.

	Brain dead (n = 30)	Not brain dead (n = 44)
Mean (range) age (y)	48.5 (18–89)	59.8 (22–90)
Female sex	15	21
Etiology of coma		
Brain hemorrhage	8	10
Traumatic injury	7	5
SAH	7	6
Ischemic stroke	4	2
Other cause	4	21
Mean \pm SD (range) time between clinical evaluation and PMD-TCD (min)	82.5 \pm 51.8 (5–178)	86.3 \pm 50.1 (8–171)

PMD-TCD = power mode transcranial Doppler;
SAH = subarachnoidal hemorrhage.

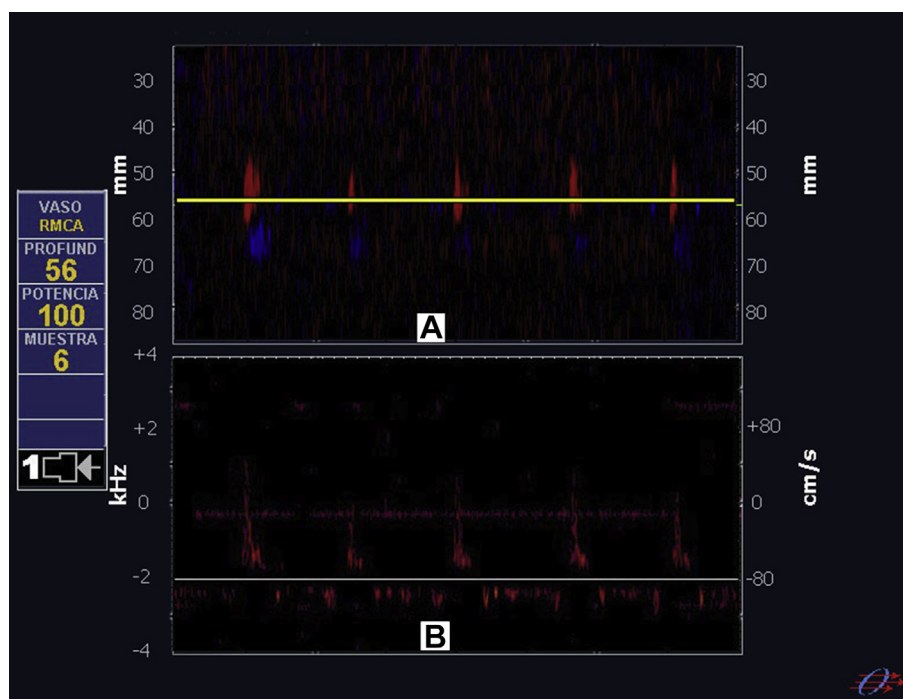


Fig. 2 Power M-mode Doppler screen of a middle cerebral artery in a patient with a severe traumatic brain injury. (A) M-mode sector of the screen. A high-resistance signal is evident in the red tracings between the depths of 45 mm and 65 mm, representing the M1 segment of the middle cerebral artery; between the depths of 60 mm and 70 mm, a blue high-resistance signal is observed from the anterior cerebral artery. (B) Doppler sector of the screen where a reverberating signal is observed.

progressive and generalized increases in intracranial pressure, which causes cerebral flow arrest. As demonstrated in previously reported cases of false positive ultrasound studies [6], BD becomes apparent a short time later.

To our knowledge, this is the first study evaluating transcranial Doppler that uses likelihood ratios as a measure of accuracy for ultrasound in the diagnosis of BD. This statistical tool has more validity than sensitivity, specificity, or positive or negative predictive power [22].

The main strength of our study is that it incorporated unselected patients who may be considered to be representative of patients with SC who are admitted to an ICU;

only two of these patients were excluded because PMD-TCD did not demonstrate blood flow; this could be explained by the absence of a neurosonological window or the true absence of blood flow. This correlates with the 5% absence of ultrasonographic windows observed in the Chilean population [23].

Our study has some limitations. Twenty-three patients could not be included because the clinical evaluation and PMD-TCD could not be carried out within less than 3 hours of each other. This is a single center experience with a single highly experienced operator and we did not test the inter-rater reliability of PMD-TCD.

Table 2 Reported studies evaluating transcranial Doppler in the diagnosis of brain death.

Reference	Technique used	n	Sensitivity (%)	Specificity (%)	Positive predictive value	Negative predictive value	Circulation evaluated
[15]	SGTCD	37	81.8	100	100	78.9	Middle cerebral artery
[16]	SGTCD	54	80	100	100	84	Ant and post
[17]	SGTCD	133	93.2	100	100	80.56	Ant and post
[18]	SGTCD	75	84.6	100	100	92.4	Middle cerebral artery
[19]	SGTCD	137	96.3	98.1	98.7	94.6	Ant and post
[20]	SGTCD	15	100	100	100	100	Middle cerebral artery
[9]	PMD-TCD	22	100	100	100	100	Ant and post
[11]	PMD-TCD	74	100	98	96.7	100	Ant and post

Ant and post = anterior circulation and posterior circulation; PMD-TCD = power mode transcranial Doppler; SGTCD = single-gate transcranial Doppler.

In conclusion, PMD-TCD is an accurate tool for the diagnosis of BD and is most likely to be more accurate than single-gate TCD. It may be used as an additional and alternative test for the diagnosis of BD, especially in developing countries.

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